

<110> Tudan, Christopher R.
 Merzouk, Ahmed
 Arab, Lakhdar
 Saxena, Geeta
 Eaves, Connie J.
 Cashman, Johanne
 Clark-Lewis
 Salari, Hassan

<120> CXCR4 AGONIST TREATMENT OF HEMATOPOIETIC CELLS

<130> SMAR012

<140> US 09/835,107

<141> 2001-04-12

<150> CA 2,305,036

<151> 2000-04-12

<150> US 60/232,425

<151> 2000-09-14

<150> CA 2,335,109

<151> 2001-02-23

<160> 34

<170> PatentIn Ver. 2.0

<210> 1

<211> 67

<212> PRT

```
<213> Homo sapiens
```

<220>

<223> SDF-1 alpha

<400> 1

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser 1 5 10 15

His Val Ala Arg Ala Asn Val Lys His Leu Lys Ile Leu Asn Thr Pro
20 25 30

Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys Asn Asn Asn Arg Gln

35 40 40 45

Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys 50 55 60

Ala Leu Asn

65

<210> 2

<211> 93

<212> PRT

<213> Homo sapiens

<220>

<223> SDF-1 Precursor, PBSF

<400> 2

Met Asn Ala Lys Val Val Val Leu Val Leu Val Leu Thr Ala Leu

1 5

10

15

Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys

20

25

30

Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys

35

40

45

Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys

50

55

60

Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln

65

70

75

80

Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met

85

90

<210> 3

<211> 93

<212> PRT

<213> Homo sapiens

<220>

<223> SDF-1 beta

<400> 3

Met Asn Ala Lys Val Val Val Leu Val Leu Val Leu Thr Ala Leu

1 5 10 15

Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys
20 25 30

Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys
35 40 45

Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys
50 55 60

Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln 65 70 75 80

Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met
85 90

<210> 4

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthesised in Laboratory: SDF-1(1-17): or CTCE9902

```
<400> 4
```

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser

1

5

10

15

His

<210> 5

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthesised in Laboratory

<400> 5

Arg Phe Phe Glu Ser His

1

5

<210> 6

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthesised in Laboratory

```
<400> 6
Lys Pro Val Ser Leu Ser Tyr Arg Cys
  1
                  5
<210> 7
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<221> DISULFID
<222> (9)
<223> Disulphide linkage between each cys at position 9
      of each monomer.
<220>
<223> Synthesised in Laboratory:
      SDF-1(1-9)2-C9/C9-cysteine dimer: or CTCE9901
<400> 7
Lys Pro Val Ser Leu Ser Tyr Arg Cys
  1
                  5
<210> 8
<211> 10
<212> PRT
<213> Artificial Sequence
```

```
<220>
<221> MUTAGEN
<222> (10)
<223> Xaa may be lysine with both the alpha and the epsilon amino groups of the lysine being associated with the covalent (amide) bond formation.
```

<220>

<223> Synthesised in Laboratory

<220>

<221> VARIANT

<222> (10)

<223> Xaa = a linking moiety between each of the cys at
pos. 9 in each SEQ ID Nos: 8 and 9

<400> 8

Lys Pro Val Ser Leu Ser Tyr Arg Cys Xaa 1 5 10

<210> 9

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

```
<223> Synthesised in Laboratory

<400> 9
Lys Pro Val Ser Leu Ser Tyr Arg Cys

1 5

<210> 10

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<221> MUTAGEN

<222> (9)

<223> Xaa may be lysine with both the alpha and the epsilon amino groups of the lysine being
```

associated with the covalent (amide) bond formation.

<223> Synthesised in Laboratory

<220>

<221> VARIANT

<222> (9)

<220>

<223> Xaa = a linking moiety between each of the arg at
 pos. 8 in each SEQ ID Nos: 10 and 11

```
<400> 10

Lys Pro Val Ser Leu Ser Tyr Arg Xaa
```

1 5

<210> 11

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthesised in Laboratory

<400> 11

Lys Pro Val Ser Leu Ser Tyr Arg

1

<210> 12

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(17)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220> <223> Synthesised in Laboratory: SDF-1(1-14)-(G)3-SDF-1(55-67) acid <400> 12

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly 1 5

10

15

Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn 20 25 30

<210> 13 <211> 31 <212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (16)..(19)

<223> spacer monomers (such as the illustrated glycine G's) may be used in variable numbers, such as 2, 3 or 4 glycines.

<220>

<223> Synthesised in Laboratory: SDF-1(1-14)-(G)4-SDF-1(55-67) acid: or CTCE0013 <400> 13

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1

5

10

15

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn

20

25

30

<210> 14

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(17)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-14)-(G)3-SDF-1(55-67) amide

<220>

<221> MOD_RES

<222> (30)

<223> AMIDATION

```
<400> 14
```

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn
20 25 30

<210> 15

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(18)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-14)-(G)4-SDF-1(55-67) amide: or CTCE0017

<220>

<221> MOD_RES

<222> (31)

<223> AMIDATION

```
<400> 15
```

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1

5

10

15

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn

20

25

30

<210> 16

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (18)..(21)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-17)-(G)3-SDF-1(55-67) acid

<400> 16

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser

1 5 10 15

His Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu

20

25

30

Asn

<210> 17

<211> 34

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (18)..(21)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<223> Synthesised in Laboratory: $SDF-1(1-17)-(G)4-SDF-1(55-67) \ acid$

<400> 17

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser

1 10 15

His Gly Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala
20 25 30

1

```
<210> 18
<211> 33
<212> PRT
<213> Artificial Sequence
<220>
<221> DOMAIN
<222> (18)..(20)
<223> spacer monomers (such as the illustrated glycine
      G's) may be used in variable numbers, such as 2, 3
      or 4 glycines.
<220>
<223> Synthesised in Laboratory:
      SDF-1(1-17)-(G)3-SDF-1(55-67) amide
<220>
<221> MOD_RES
<222> (33)
<223> AMIDATION
<400> 18
Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu Ser
```

10

15

His Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu
20 25 30

Asn

<210> 19

<211> 34

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (18)..(21)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-17)-(G)3-SDF-1(55-67) amide

<220>

<221> MOD_RES

<222> (34)

<223> AMIDATION

<400> 19

His Gly Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala
20 25 30

Leu Asn

<210> 20

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(18)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<221> DOMAIN

<222> (24)..(28)

<223> Cyclized, for example glutamate (E) and lysine (K) residues may be joined by side chain cyclization using a lactam formation procedure.

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn
20 25 30

<210> 21
<211> 31
<212> PRT
<213> Artificial Sequence

1

<221> DOMAIN <222> (15)..(18)

<220>

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>
<221> DOMAIN
<222> (20)..(24)

<223> Cyclized, for example glutamate (E) and lysine (K) residues may be joined by side chain cyclization

using a lactam formation.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-14)-(G)4-SDF-1(55-67)-K20/E24-cyclic acid

<400> 21

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn

20 25 30

<210> 22

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(18)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<221> DOMAIN

<222> (24)..(28)

<223> Cyclized, for example (E) and lysine (K) residues
 may be joined by side chain cyclization using a
 lactam formation procedure.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-14)-(G)4-SDF-1(55-67)-E24/K28-cyclic

amide: or CTCE0022

<220>

<221> MOD_RES

<222> (31)

<223> AMIDATION

<400> 22

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn

20 25 30

<210> 23

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<223> Clyclized, for example glutamate (E) and lysine (K) residues may be joined by side chain cyclization using a lactam formation procedure.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-14)-(G)4-SDF-1(55-67)-K20/E24-cyclic

amide: or CTCE0021

<220>

<221> MOD_RES

<222> (31)

<223> AMIDATION

<400> 23

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn

20 25 30

<210> 24

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(18)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<221> DOMAIN

<222> (20)..(24)

<223> Internal cyclization of peptides of the invention may be in alternative positions, or between substituted amino acids. The nature of the cyclic linkage may also be varied.

<220>

<223> Synthesised in Laboratory: SDF-1(1-14)-(G)4)-SDF-1(55-67)-K20/D24-cyclic acid

<400> 24

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Leu Lys Trp Ile Gln Asp Tyr Leu Glu Lys Ala Leu Asn
20 25 30

<210> 25

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(18)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<221> DOMAIN

<222> (20)..(24)

<223> Internal cyclization of peptides of the invention may be in alternative positions, or between substituted amino acids. The nature of the cyclic linkage may also be varied.

<220>

<220>

```
<221> MOD_RES
<222> (31)
<223> AMIDATION
<400> 25
Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly
  1
```

Gly Gly Leu Lys Trp Ile Gln Asp Tyr Leu Glu Lys Ala Leu Asn

25

10

15

30

<210> 26 <211> 31 <212> PRT <213> Artificial Sequence

20

5

<221> DOMAIN <222> (15)..(18)

<220>

<223> spacer monomers (such as the illustrated glycine G's) may be used in variable numbers, such as 2, 3 or 4 glycines.

<220> <221> DISULFID <222> (9)..(11)

<223> cystein residues may for example be involved in bridge formation

```
<220>
```

<223> Synthesised in Laboratory:

SDF-1(1-14)-(G)4-SDF-1(55-67)-C9/C11-cyclic acid

<400> 26

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn

20 25 30

<210> 27

<211> 31

<212> PRT

<213> Artificial Sequence

<220>

<221> DOMAIN

<222> (15)..(18)

<223> spacer monomers (such as the illustrated glycine
 G's) may be used in variable numbers, such as 2, 3
 or 4 glycines.

<220>

<221> DISULFID

<222> (9)..(11)

<223> Cysteine residues may for example be invloved in

bridge formation.

<220>

<223> Synthesised in Laboratory:

SDF-1(1-14)-(G)4-SDF-1(55-67)-C9/C11-cyclic amide

<220>

<221> MOD_RES

<222> (31)

<223> AMIDATION

<400> 27

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn

20 25 30

<210> 28

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthesised in Laboratory: SDF-1(1-14)-(G)4-MIP-1 alpha(36-50)amide

<220>

<221> MOD_RES

```
<222> (33)
<223> AMIDATION
<400> 28
```

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Ser Lys Pro Gly Val Ile Phe Leu Thr Lys Arg Ser Arg Gln
20 25 30

Val

<220>

<210> 29
<211> 58
<212> PRT
<213> Artificial Sequence

<223> Synthesised in Laboratory: SDF-1(1-14)-(G)4-MIP-1 alpha(11-50)-acid or amide

<221> MOD_RES
<222> (58)
<223> AMIDATION

<400> 29

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe
20 25 30

Ile Ala Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Gly Val

Ile Phe Leu Thr Lys Arg Ser Arg Gln Val
50 55

<210> 30

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthesised in Laboratory: SDF-1(1-14)-(G)4-MIP-1 alpha(56-70)-acid or amide

<220>

<221> MOD_RES

<222> (33)

<223> AMIDATION

<400> 30

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1

5

10

15

Gly Glu Glu Trp Val Gln Lys Tyr Val Asp Asp Leu Glu Leu Ser

20

25

30

Ala

<210> 31

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<221> SITE

<222> (9)

<223> Lysine bridge dimer between each arg at each position 8 in SEQ ID NO 31 and SEQ ID NO 32

<220>

<223> Synthesised in Laboratory: SDF-1(1-8)2-lysine bridge dimer: or CTCE9904

<220>

<221> MOD_RES

<222> (9)

<223> AMIDATION

```
<400> 31
```

Lys Pro Val Ser Leu Ser Tyr Arg Lys

1 5

<210> 32

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<221> SITE

<222> (8)

<223> bonds with SEQ ID NO 31 by forming lysine bridge
 dimer between each arg of each position 8 of SEQ
 ID NO 31 and SEQ ID NO 32

<220>

<223> Synthesised in Laboratory: SDF-1(1-8)2-lysine bridge dimer: or CTCE9904

<400> 32

Lys Pro Val Ser Leu Ser Tyr Arg

1 5

<210> 33

<211> 40

<212> PRT

<213> Artificial Sequence

```
<220>
<223> Synthesised in Laboratory
```

<400> 33

Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile Ala Asp Tyr Phe 1 5 10 15

Glu Thr Ser Ser Gln Cys Ser Lys Pro Gly Val Ile Phe Leu Thr Lys Arg 20 25 30 35

Ser Arg Gln Val

<210> 34

<211> 33

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthesised in Laboratory: SDF-1(1-14)-(G)4-MIP-1 alpha(36-50)-acid

<400> 34

Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Gly Gly

1 5 10 15

Gly Gly Ser Lys Pro Gly Val Ile Phe Leu Thr Lys Arg Ser Arg Gln
20 25 30

Val